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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/781,581	02/18/2004	Liam Seery	8912/2015	2809

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EXAMINER	
BORGEEST, CHRISTINA M	
ART UNIT	PAPER NUMBER
1649	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/781,581	SEERY ET AL.	
	Examiner	Art Unit	
	Christina Borgeest	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *13 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *4-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 13-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

A notice of non-compliance was mailed 12 January 2007 because the Examiner asserted that amended claim 1 and newly submitted claims 13-14 were directed to an invention distinct from the elected invention. However, after phone conversations with Applicants' attorney on 9 and 12 February 2006, the Examiner has decided to withdraw the Notice of Non-compliance. The Notice of Non-compliance mailed 12 January 2007, is hereby vacated and Applicants are relieved of the requirement to respond.

Applicants amendment filed 13 October 2006 is acknowledged. Claims 1 and 3 are amended and claims 13-14 are new. Claims 4-12 are withdrawn. Claims 1-3 and 13-14 are under examination.

Priority

Applicants intention to submit a certified copy of the 0301566.6 application as required by 35 U.S.C. 119(b) is acknowledged. The copy has not yet received, thus the objection will remain of record until the certified copy is received.

Objections/Rejections Withdrawn

Specification

The objection to the disclosure to because it contains an embedded hyperlink and/or other form of browser-executable code is withdrawn in response to Applicants' amendment of the specification filed 13 October 2006.

Claim Objections

The objection to claims 1-3 for encompassing non-elected subject matter is withdrawn in response to Applicants' amendment of the claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 1-3 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in response to Applicants' amendment of the claim.

Claim Rejections - 35 USC § 102

The rejection of claims 1-3 under 35 U.S.C. 102(b) as being anticipated by Dewaste et al. (Biochem J. 2000; 352: 343-351) is withdrawn in response to Applicants' amendment of the claims. The claims no longer encompass a screening method for identifying an agent that modulates the function of SEQ ID NO: 226 comprising providing a preparation containing SEQ ID NO: 226, wherein the preparation containing the protein comprises a cell expressing the protein shown in SEQ ID NO: 226, incubating the cell expressing the protein in SEQ ID NO: 226 with a test agent to be

screened under conditions that permit binding of the test agent to SEQ ID NO: 226, and determining whether the test agent interacts with SEQ ID NO: 226 by determining phosphotransferase activity of the protein kinase, thus Dewaste et al. no longer anticipates the claims.

Objections Maintained/New Objections/Rejections

Specification

The objection to the specification because Table 1B refers to the proteins by GenBank number is maintained. Applicants argue that sequence rules pertain to the disclosure of sequences, not protein numbers and GenBank changes can be tracked and related to the filing date of the application, however, this is not persuasive and the objection is maintained. The specification does not refer to the date on which the GenBank sequences were accessed, so it is also unclear whether the sequences were those that existed on the filing date or previous incarnations thereof.

Claim Objections

Claim 3 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 3 no longer limits claim 1, because claim 3 recites determining ***whether the test agent interacts with the protein by detecting a change in the phosphotransferase activity of ITPKC***,

whereas claim 1 recites determining ***whether the test agent interacts with the protein by detecting the presence or absence of an apoptotic signal***, and phosphotransferase activity is not recited in the list of apoptotic assays, thus claim 3 no longer limits the step recited in claim 1 (as amended).

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 13-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (1) carrying out the claimed method in cells, wherein the method of identifying an agent that modulates the full length of the protein encoded by the gene for inositol 1,4,5-triphosphate 3-kinase C (ITPKC) or (2) a method of identifying an agent that modulates the function of full length protein ITPKC, comprising providing a preparation containing said ITPKC; incubating the preparation with a test agent to be screened under conditions to permit binding of the test agent to ITPKC; determining whether the test agent interacts with ITPKC by detecting the presence or absence of a an apoptotic signal, selected from the group consisting of: caspase activation, does not reasonably provide enablement for the methods as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." (See In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 Fed. Cir. 1988) These factors include, but are not limited to: (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

First, with regard to the rejection made in the previous Office action mailed 13 June 2006, a rejection was made under 35 U.S.C. 112, first paragraph, because the specification, while being enabling a method of identifying an agent that modulates the full length of the protein encoded by the gene for ITPKC, does not reasonably provide enablement for a method of identifying an agent that modulates the protein fragment as shown in SEQ ID NO: 226. Applicants amended the claim to recite modulates the function of "ITPKC", however, the specification defines the apoptosis associated proteins broadly; for instance, see paragraph [0038]:

In an additional aspect, the invention features a method of modulating apoptosis in a cell, where the method includes: (a) transforming into the cell a double-stranded nucleic acid sequence encoding a polypeptide having at least 80% sequence identity with a polypeptide having a sequence as set out in Table 1B, where the nucleic acid sequence is operably linked to a regulatory sequence; and (b) culturing the cell under conditions whereby the nucleic acid sequence is expressed; thereby modulating apoptosis in the cell.

Thus for this reason, the claims, including new claims 13-14, still encompass fragments of ITPKC that may be non-functional in the claimed methods, and the issues raised in the original rejection are still applicable here.

Regarding claims 1-3, apoptosis is programmed cell death (see definition at p. 489, left column, 1st paragraph and Figure 1 of Saikumar et al. Am J. Med. 1999; 107: 489-506). As is clear from Figure 1 of Saikumar et al., cell death requires the presence of a cell. Amended claim 1 recites "[a] method of identifying an agent that modulates the function of inositol-1, 4 5-triphosphate 3-kinase C (ITPKC), comprising providing ***a preparation*** containing said ITPKC; incubating ***the preparation*** with a test agent to be screened under conditions to permit binding of the test agent to ITPKC; determining whether the test agent interacts with ITPKC by detecting the presence or absence of a ***an apoptotic signal, selected from the group consisting of: caspase activation, DNA fragmentation, cell death, lack of cell proliferation, amount of G1 DNA, change in mitochondrial membrane potential, or externalization of phosphatidylserine***, and the signal generated from the interaction of the agent with ITPKC, and thereby determining whether the test agent modulates the function of ITPKC. The measurement of apoptotic signals recited in claim 1 (cell death, lack of cell proliferation, amount of G1 DNA, change in mitochondrial membrane potential and externalization of phosphatidylserine require presence of a cell. A "preparation" encompasses a cell free system or some other type of non-cellular assay.

The literature does provide some examples of cell-free systems in apoptosis studies for studying caspase activation. For instance, Han et al. (JBC. 1997; 272:

13432-13436), teaches a cell fee system in which the proteolytic processing of caspase-3 precursor protein was studied. Likewise, Zhou et al. (Journal Cell Biol. 2000; 151: 483-494) teaches a cell free system in which caspase activation is studied. However, Zhou et al. also teach the interaction PI 3-kinase (which is not the same protein as ITPKC) with L7 294002 in HMN1 cells; i.e., although caspase activation was studied in cell free systems, the claims require the study of the interaction between ITPKC and a test agent, and neither the specification nor the literature teach a cell-free system in which a test agent is screened to permit binding of the test agent to ITPKC and measuring apoptosis. Furthermore, the art is unpredictable and complex concerning ITPKC (see Pattni et al. Cell Signal. 2004; 16: 643-654). First, little is known about the catalytic mechanism of ITPKC, though it is known that the activity is regulated by phosphorylation of the enzyme (see p. 646). It is thought that the subcellular localization of ITPKC (as well as the A and B isoforms) is important to its function, since its substrate acts in specific locations within the cell (see p. 647, left column, 2nd paragraph): "[for] example, cells expressing both the [B and C isoforms] would be able to evoke an [ITPK activity] under different cellular conditions and in different cellular compartments." This suggests that it is important to study ITPKC in the cell, since localization is important to its function. Finally, the intracellular location of the C isoform is not precisely known; see p. 649, right column, where it says Erneux and colleagues report no membrane association (thus cytosolic) and Nalaskowski and colleagues show that the kinase shuttles between the nucleus and the cytosol. This reference and the passages cited herein demonstrate the unpredictability of the art concerning ITPKC,

thus the person of skill in the art would not have guidance as to how to create the cell free assay encompassed by the claims (identifying a test agent that modulates the function of ITPKC in a cell free system by detecting the presence or absence of an apoptotic signal).

Due to the large quantity of experimentation necessary to create a cell-free assay capable of carrying out the assay as claimed, the lack of direction/guidance presented in the specification regarding and the absence of working examples directed to the same, the complex nature of the invention, the contradictory state of the prior art, (the level of skill of those in the art), the unpredictability of the concerning ITPKC (see Pattni et al., discussed above), and the breadth of the claims which fail to recite limitations on the type of assay (cellular or cell-free), undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Dewaste et al. (Biochem J. 2000; 352: 343-351—cited in prior Office action mailed 13 June 2006). The new claims 13-14 recite a method for identifying an agent that modulates the function of ITPKC comprising providing; incubating the preparation with a

test agent to be screened under conditions that permit binding of the test agent to ITPKC, wherein the test agent is selected from the group consisting of low molecular weight organic molecule, an antibody or antibody fragment, an antisense oligonucleotide, an small inhibitory dsRNA and a ribosyme; determining whether the test agent interacts by ITPKC by detecting the presence or absence of a signal generated from the interaction of the agent with ITPKC, and thereby determining whether the test agent modulates the function of ITPKC, wherein determining whether the test agent interacts with ITPKC is by detecting a 75% change in a signal generated from the interaction of the agent with ITPKC.

Dewaste et al. teach a method of expressing ITPKC in both *E. coli* and COS-7 cells (see p 344, right column, last paragraph and p. 345, left column, last paragraph), treating with calmodulin (i.e., meets limitation of low molecular weight small organic molecule test agent—see p. 348, right column, 2nd paragraph) and measuring kinase activity (i.e., determining phosphotransferase activity of the protein kinase—see p. 349, Figure 8a, upper panel). The kinase activity after calmodulin treatment is about 6.25 nmol/min/ml in 8a, upper panel. The kinase activity measured in Panel B after vehicle and Ca++ treatment is between 50-125 nmol/min/ml. Absent evidence to the contrary, administration of calmodulin effected at least a 75% change in kinase activity as compared with control or varying levels of Ca++ The claims are encompassed by the teachings of Dewaste et al., and do not contribute anything over the prior art.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is 571-272-4482. The examiner can normally be reached on 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Elizabeth C. Kemmerer

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PRIMARY EXAMINER